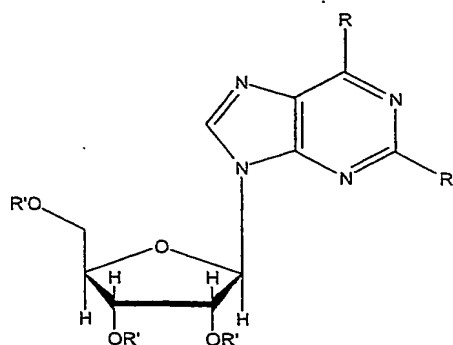
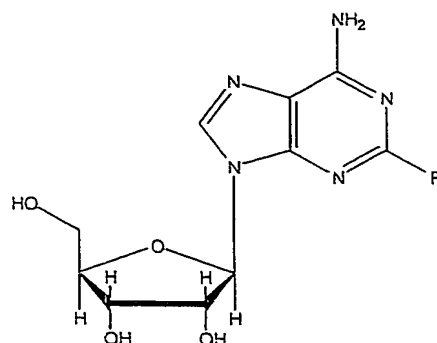


Claims

1. A method of synthesis of a 2-substituted adenosine of formula I which comprises converting a compound of formula II to a compound of formula I:

**II****I**

wherein:

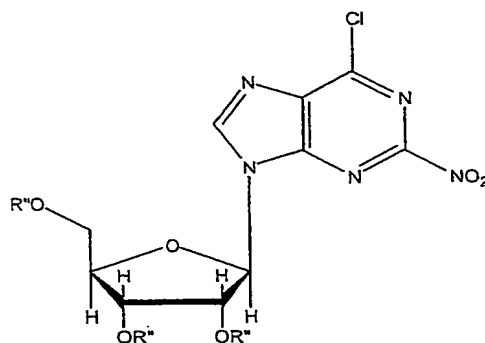
R is C₁₋₆ alkoxy (straight or branched), a phenoxy group (unsubstituted, or mono-, or di-substituted by halo, amino, CF₃-, cyano, nitro, C₁₋₆ alkyl, or C₁₋₆ alkoxy), a benzyloxy group (unsubstituted, or mono-, or di-substituted by halo, amino, CF₃-, cyano, nitro, C₁₋₆ alkyl, or C₁₋₆ alkoxy), or a benzoyl group (unsubstituted, or mono-, or di-substituted by halo, amino, CF₃-, cyano, nitro, C₁₋₆ alkyl, or C₁₋₆ alkoxy);

R' = H, or a protecting group.

2. A method according to claim 1, wherein R = methoxy, ethoxy, propoxy, butoxy, pentyloxy, hexyloxy, phenoxy, benzyloxy, or benzoyl.
3. A method according to claim 1 or 2, wherein R' is a protecting group that can be removed under conditions that replace the R group with an amino group at the 6-position of the purine component of the compound of formula II.
4. A method according to claim 3, wherein the compound of formula II is converted to the compound of formula I in a single reaction step.
5. A method according to any preceding claim, wherein the protecting group is

acetyl or benzoyl, and the compound of formula II is converted to the compound of formula I by treatment with ammonia.

6. A method according to claim 1 or 2, wherein R' is H, and the compound of formula II is aminated to form the compound of formula I.
7. A method according to claim 6, wherein the compound of formula II is aminated by heating the compound in a solution of ammonia and then cooling the solution to precipitate the compound of formula I.
8. A method according to any preceding claim, which further comprises isolating the compound of formula I produced.
9. A method according to any preceding claim, which further comprises converting a compound of formula III to a compound of formula II:

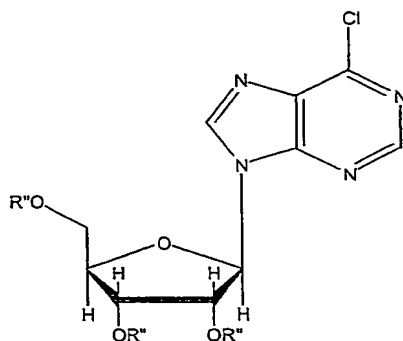


III

wherein R'' is a protecting group, preferably acetyl or benzoyl.

10. A method of synthesis of a compound of formula II which comprises converting a compound of formula III to the compound of formula II.
11. A method according to claim 9 or 10, wherein the compound of formula III is alkoxylated or benzoylated to form the compound of formula II.

12. A method according to any of claims 9 to 11, wherein the compound of formula III is triacetoxo 2-nitro-6-chloroadenosine.
13. A method according to claim 12, wherein triacetoxo 2-nitro-6-chloroadenosine is methoxylated using sodium methoxide in methanol as methoxylating reagent.
14. A method according to any of claims 9 to 13, which further comprises isolating the compound of formula II produced.
15. A method according to any of claims 9 to 14, which further comprises converting a compound of formula IV to a compound of formula III:

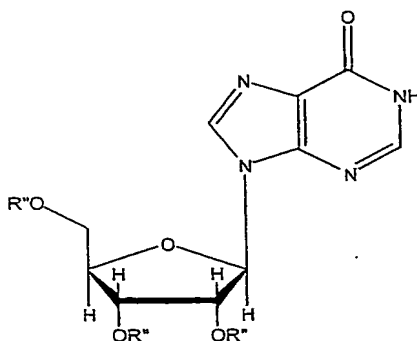


IV

wherein R'' is a protecting group, preferably acetyl or benzoyl.

16. A method according to claim 15, wherein the compound of formula IV is nitrated to form the compound of formula III.
17. A method according to claim 15 or 16, which further comprises isolating the compound of formula III produced;
18. A method according to any of claims 15 to 17, wherein the compound of formula IV is triacetoxo 6-chloroadenosine, and the compound of formula III is triacetoxo 2-nitro-6-chloroadenosine.

19. A method according to claim 18, wherein triacetoxo 6-chloroadenosine is nitrated to triacetoxo 2-nitro-6-chloroadenosine using tetrabutyl ammonium nitrate (TBAN) or tetramethyl ammonium nitrate (TMAN) as nitrating reagent.
20. A method according to claim 19, which further comprises reducing the amount of tetrabutyl ammonium (TBA) or tetramethyl ammonium (TMA) impurities contaminating the triacetoxo 2-nitro-6-chloroadenosine.
21. A method according to claim 20, wherein the amount of TBA or TMA impurities is reduced by triturating the triacetoxo 2-nitro-6-chloroadenosine from isopropanol or ethanol, and washing the triturated triacetoxo 2-nitro-6-chloroadenosine with a mixture of water and ethanol.
22. A method according to any of claims 15 to 21, which further comprises converting a compound of formula V to a compound of formula IV:



V

wherein R'' is a protecting group, preferably acetyl or benzoyl.

23. A method according to claim 22, wherein the compound of formula V is chlorinated to form the compound of formula IV.
24. A method according to claim 22 or 23, wherein the compound of formula V is triacetoxo inosine, and the compound of formula IV is triacetoxo 6-chloroadenosine.

25. A method according to claim 24, wherein triacetoxy inosine is chlorinated using thionyl chloride or POCl_3 as chlorinating reagent.
26. A method according to any of claims 22 to 25, which further comprises isolating the compound of formula IV produced.
27. A method according to any of claims 22 to 26, which further comprises converting inosine to a compound of formula V.
28. A method according to claim 27, wherein inosine is acetylated or benzoylated to form the compound of formula V.
29. A method according to claim 27 or 28, wherein the compound of formula V is triacetoxy inosine.
30. A method according to claim 29, wherein inosine is acetylated using acetic anhydride as acetylating reagent.
31. A method according to any of claims 27 to 30, which further comprises isolating the compound of formula V produced.
32. A method of synthesis of spongiosine which comprises the steps shown in scheme 1.
33. A method of synthesis of spongiosine which is substantially as described with reference to steps 1 to 5 of the Example.
34. A 2-substituted adenosine of formula I synthesized by a method according to any of claims 1-9, or 11-33.
35. A method of synthesis of 2,6-dimethoxy adenosine which is substantially as described with reference to steps 1 to 4 of the Example.

36. A compound of formula II synthesized by a method according to any of claims 10 to 31, or 35.
37. Use of a compound of formula II, III, IV, V, triacetoxy 2-nitro, 6-chloroadenosine, triacetoxy 6-chloroadenosine, triacetoxy inosine, or inosine in the synthesis of a compound of formula I.
38. Use of a compound of formula III, IV, V, triacetoxy 2-nitro, 6-chloroadenosine, triacetoxy 6-chloroadenosine, triacetoxy inosine, or inosine in the synthesis of a compound of formula II.
39. A method of producing a nitrated substituted adenosine which comprises nitrating a substituted adenosine using TBAN or TMAN, and reducing the amount of TBA or TMA impurity contaminating the nitrated substituted adenosine.
40. A method according to claim 39, wherein the amount of TBA or TMA impurity is reduced by triturating the nitrated substituted adenosine from isopropanol or ethanol, and washing the triturated product with a mixture of water and ethanol.